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EXAMINER	
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RECORD OF ORAL HEARING

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte MARIE-CLAUDE GINGRAS and JUDITH F. MARGOLIN

Appeal 2007-3749
Application 10/021,509
Technology Center 1600

Oral Hearing Held: March 6, 2008

Before TONI R. SCHEINER, DEMETRA J. MILLS, and ERIC B. GRIMES, *Administrative Patent Judges*.

ON BEHALF OF THE APPELLANTS:

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ALSO PRESENT:
MARIE-CLAUDE GINGRAS

The above-entitled matter came on for hearing on Thursday, March 6, 2008, commencing at 1:06 p.m., at the U.S. Patent and Trademark Office, 600 Dulany Street, Alexandria, Virginia, before Christine L. Loeser, Notary

Public.

JUDGE SCHEINER: Good afternoon. As you can see, we have some observers today behind you. They are from the patent academy. Whenever you are ready. Would you like to introduce your colleague?

DR. ROUSSEL: Yes. We can sit or we have to stand up?

JUDGE SCHEINER: Your preference.

DR. ROUSSEL: I'm Dr. Eugene Roussel. I am the co-owner of Geneprint Corporation, the assignee of this patent. I have written all the positions for this patent the past three years.

This is the primary inventor, Dr. Gingras. She is at the Baylor College of Medicine in Houston.

JUDGE SCHEINER: Welcome.

DR. ROUSSEL: Thank you.

JUDGE SCHEINER: Whenever you are ready.

DR. ROUSSEL: It's pretty simple. It's all about Trem-1 receptor. Trem-1 receptor is a receptor present on macrophages. It is a receptor of activation.

When Trem-1 is activated by its ligand, it activates macrophage that then will lead to activation of the immune system.

Trem-1sv, which is the main claim of this patent, is Trem-1 receptor without the anchorage membrane portion. So it makes the Trem-1 receptor soluble, if you will. It's called Trem-1 splice variant and it is a variant because, as I said, the tail that allowed the receptor to be anchored is deleted so it has the same biological function.

So when Trem-1 is activated by this ligand, the macrophage is activated. If you use Trem-1sv, it has the competitive inhibitor. You can

decrease the activation by capturing the ligand before the Trem-1 reaches its own macrophages. Therefore, you can modulate a response like that.

That is about -- so what we are claiming is the use of Trem-1sv as an immuno modulator, to modulate immune response.

An example, if you have a lot of ligand, an excess of ligand that leads to an excess activation of macrophages, it will lead in the systemic overdrive and will cause what we call general inflammation or septic shock.

If you provide an effective amount of Trem-1sv, that will capture the ligand before reaction with Trem-1, we can control the activation of macrophages or block it completely and prevent septic shock.

So we are claiming basically Trem-1 has a new medicant to modulating immune system diseases.

JUDGE SCHEINER: Why don't we move on to what the examiner's rejections were? Can we discuss the new matter rejection first, please?

DR. ROUSSEL: We can discuss whatever you want. We have been rejected on the lack of enablement, prior art, new matter in the claims.

JUDGE SCHEINER: Why don't we do new matter, enablement, and if there's time we can go on to prior art.

DR. ROUSSEL: Just to begin, there is -- we have nine claims. None of them -- all of them are supported by at least two paragraphs in our specification. I can provide you in detail all the paragraphs that support each of our claims.

JUDGE SCHEINER: I believe those are in the briefs. They are paragraphs somewhere around 50. Is that correct?

DR. ROUSSEL: May I suggest that we go claim by claim?

JUDGE SCHEINER: Actually, you have only argued claim 1 in the brief, so we are going to confine ourselves to claim 1.

DR. ROUSSEL: Okay.

JUDGE SCHEINER: Or actually, I think that the limitations of amino acids -- is it 14 to -- I think there are two endpoints that the examiner was concerned about, 36 to 114, and then in claim 1, it's amino acids 1 to 136, so why don't we talk about the support for those endpoints?

DR. ROUSSEL: Well, first of all, we have described the sequence in detail in figure 4 where it is very well demonstrated that the sequence -- the structure of this molecule is, as in the figure 1, contained a loop, and the presence of this loop is highlighted by the box where the hinge is for each side of the loop.

And our sequence is basically 36 to 114, which is basically this loop that is the biological active site of this peptide.

JUDGE SCHEINER: That is in the specification?

DR. ROUSSEL: That is described in the specification in figure 4. In figure 1, there is a series of paragraphs -- that's 8, 10, 11, 12 to 17, 50, 55, 69, 80, 105 -- and we have submitted also the sequence. We have submitted --

JUDGE SCHEINER: I think SEQ ID number 2. Does that -- that contains also the transmembrane domain?

DR. ROUSSEL: Yes. SEQ-ID number 2 is for the splice variant. It would not contain the --

JUDGE SCHEINER: Oh, I see.

DR. ROUSSEL: SEQ-ID number 2 is for the splice variant. It doesn't contain the anchorage part.

JUDGE SCHEINER: Okay. All right. I'm sorry. You said paragraphs 50 -- the last one I jotted down was 55, I think.

DR. ROUSSEL: What we describe basically in here, we have presented a sequence in detail in figure 4, and then we describe the variant that can be made from that sequence, and those are described in the section polypeptide of the patent which start at paragraph 50.

That's the definition, and then we have page 14 where we talk about the polynucleotide and we describe the type of polynucleotide that can code for the peptide. And then if you go into the section polypeptide, page 18, there is paragraphs 69 to 81 that specify all the variant that can be made.

JUDGE SCHEINER: I see here that the first 136 amino acids of the splice variant are identical to the Trem-1 receptor for 136 amino acids, so where does the cut-off -- I understand that these cut-offs -- the cut-off points 36 to 114 were added by amendment; is that correct?

DR. ROUSSEL: Yes.

JUDGE SCHEINER: Yes, okay. So what I'm asking is where the specific support for those -- it doesn't have to be a number, of course, but the specific support for that cut-off. I think that's what the examiner was concerned about.

DR. ROUSSEL: The specific for that cut-off is this. We have demonstrated -- we have described in this specification that this molecule is in the same family that the immunoglobulin and the immunoglobulin have loop domain. The loop domain is known to be from 36 to 114.

And we talked about the loop domain in paragraph 70, page 18, and then we present it in figure 1, and then we give the specifications of the [?] in figure 4.

JUDGE SCHEINER: Why don't we move on to the enablement rejection then? For that, I think what we are most interested in is enablement of the polypeptide mimetics.

DR. ROUSSEL: Okay. We have, as you can see, this patent is about immunology and the inflammation. There is 180 paragraphs on it. And if we start right from the beginning, we can define pretty much what the immune response is and also inflammation response.

We have specifically provided the work of Sebastian Gibot as well as work of Bouchon that demonstrates specifically that if you have the biological site, which means the Trem-1 without the tail, in terms of the work of Bouchon, he cut the Trem-1 -- cut the tail of Trem-1 and he put in an FC there.

JUDGE SCHEINER: What was reason for the FC? Do you know?

DR. ROUSSEL: To make it soluble. And when you use that, you are supposed to prevent and cure septic shock in mice.

Second, when Sebastian Gibot did the same thing, but instead -- and that is a proof that specifically includes our claim number 3 -- he just put -- he just took a peptide inside the loop on one edge. It was a peptide of 17 amino acids that contained biological activities enough to prevent septic shock in mice.

That is the reference to 2004 in the record. May I also quote a reference off record?

JUDGE SCHEINER: I prefer you didn't. It's not of record.

What I would like you to do is walk through Bouchon, if I'm pronouncing that correctly, and show us how that tracks your disclosure,

because I think that the argument is that Bouchon, although it is post-filing, it is evidence that the experiments you propose in the specification would have a certain result.

The declaration was a little brief, it just said the experiments were similar to what you proposed in the specification, so if you could walk through that for us, please.

DR. ROUSSEL: It's easy. If you go to page 1106, figure 5, and you look at the upper graph, panel A.

JUDGE SCHEINER: If you could just hold on a second. I have the papers mixed up a little bit here. Sorry. Have it now.

DR. ROUSSEL: We are always talking about the loop, the biological active portion of the molecule. Bouchon took Trem-1, including the loop, and cut the tail, put in FC to make it soluble and then injected it in mice.

When he used LPS to induce septic shock, and he provided the molecule, if you took panel A, the percentage of survival, you can see that those 80 percent survival, those are the open track.

JUDGE SCHEINER: I understand what Bouchon did. What I would like to know is where it tracks what you propose in the specification, if you could point that out.

DR. ROUSSEL: If you go into the treatment, page 25, and then we talked about it, 97, 98, specifically 98, the compound was administered to result in modification of the immune response. We have defined what modification is earlier where it can be an increase or a decrease of the immune response.

We describe in 101 Trem-1 splice variant down regulating the

immune response by competing with the full Trem-1 receptors for the ligand that binds Trem-1.

JUDGE SCHEINER: Let me interrupt for a second. Again, we are talking about the mimetics, not so much the pieces of Trem-1, of the soluble receptor, but the mimetics which would be functional. Actually, I don't see that mimetics are defined. The term is used.

DR. ROUSSEL: Functional equivalent?

JUDGE SCHEINER: As functional equivalents. The functional equivalent --

DR. ROUSSEL: Would be like the small peptide that Gibot used.

JUDGE SCHEINER: So it competes for the ligand for cell surface membrane receptor. We don't know what that is at that time. Why doesn't that matter if you are making a mimetic?

DR. ROUSSEL: I am not sure I understand the question.

JUDGE SCHEINER: You are using pieces of -- if you are using smaller pieces of the soluble receptor, you test for that activity, but when you are making a peptide mimetic, and we don't really have a definition of what mimetic is except it acts like a soluble receptor.

DR. ROUSSEL: Yes. It has biological activity.

JUDGE SCHEINER: So you are going to test it in exactly the same -- your position is you would test it in exactly the same way you would test the shorter versions of the receptor?

DR. ROUSSEL: Yes. If you take the paper of Bouchon and replace it with the peptide of Gibot, you have a mimetic. That's example of mimetic.

JUDGE SCHEINER: That was a shorter version.

DR. ROUSSEL: It's a shorter version.

JUDGE SCHEINER: But mimetic covers more than that, right?

DR. ROUSSEL: It can.

DR. GINGRAS: As long as you keep the active binding function.

DR. ROUSSEL: As long as you maintain --

JUDGE SCHEINER: The ligand binding.

DR. ROUSSEL: -- the ligand binding. And we talked about the variant in our patent, paragraph 55.

JUDGE GRIMES: So the term "mimetic" would include both fragments of the naturally occurring sequence as well as variants.

DR. ROUSSEL: Yes. As we have described in our specification in paragraph 55 and later on in page 18, paragraph 73 and paragraph 80, where we demonstrated it's known in the art how to generate these variants.

JUDGE SCHEINER: Okay. Do you have any questions?

JUDGE MILLS: No.

JUDGE SCHEINER: Do you want to move on to the art rejections then? Unless you have more you want to say on enablement.

DR. ROUSSEL: No. I think we have answered your question and I think we have got support for all of our claims. We have got support for all of your questions. Our specifications are very well detailed, and we have provided proof of working evidence.

And I would like to point out, however, on the paper of Gibot,

that it has been shown that patients recovering better in human -- patients recovering better from the septic shock have a higher rate of soluble Trem-1, which is another support that this thing works in humans.

JUDGE SCHEINER: Okay.

DR. ROUSSEL: This reference is in record page 1424, second column.

JUDGE SCHEINER: I have it here.

DR. ROUSSEL: Okay. So you want us to discuss the rejection according to prior art?

JUDGE SCHEINER: Mm-hmm. There were two, one or two rejections like that?

DR. ROUSSEL: There was 110 and 526. In 110, these people claim to treat cancer with Trem-1-SD. We claim to treat septic shock and autoimmune disease. We don't claim to treat cancer.

JUDGE SCHEINER: That was 010?

DR. ROUSSEL: Yes. We are talking also about the peptides. We have defined the biological site of the peptide. They are having only the immune sequence.

JUDGE SCHEINER: Only DNA and only treating cancer.

DR. ROUSSEL: Yes.

JUDGE SCHEINER: Which sequence is it in?

DR. ROUSSEL: It would be sequence number 2.

JUDGE SCHEINER: No. In the patent. Do you know offhand?

DR. ROUSSEL: In the patent? Oh, I don't have copy of the patent in front of me.

JUDGE SCHEINER: That's okay. We have it somewhere in the record.

DR. ROUSSEL: Yes, it is. They also claim that it involve the lymphocytes. We claim it involves the macrophages.

JUDGE SCHEINER: We are still on 010.

DR. ROUSSEL: Yes. Do you have other question on 010?

JUDGE SCHEINER: I don't.

DR. ROUSSEL: Okay. Patent 526, this is a patent that contain a whole bunch of EST. The patent is not reduced to practice and would require lots of experimentation. We have in our patent, we are talking about the peptide.

We have defined the biological site. We have -- we have reduced practice in terms of administration, treatment, mechanism. We have a clear teaching and we do not remove anything from the public by having this patent granted to us because the other patent, 526, is basically not reduced to practice.

There is no definition of the polypeptide, and the whole description is six paragraphs long. We have a patent with 188 paragraphs, if not more, and it's fundamentally about inflammation.

JUDGE SCHEINER: Okay. Questions?

JUDGE MILLS: No questions.

JUDGE SCHEINER: Is there anything else you wanted to add?

DR. ROUSSEL: No.

JUDGE SCHEINER: I think we understand the issues.

DR. ROUSSEL: We are done?

JUDGE SCHEINER: We are done unless you have something

else to add.

DR. ROUSSEL: We would just like to add one thing is that we are waiting -- this prosecution has been going on for six years. We would really appreciate -- we understand what the USPTO has done to help us build, if you want, a better patent.

At this point, we would appreciate having the patent being issued so we can move forward in developing a new medication for patients suffering septic shock and autoimmune disease. It is a disease in the United States that have 500,000 cases per year and the survival rate is 70 percent. No, the death rate is 70 percent within one year.

JUDGE SCHEINER: All I can promise you is we will get our decision out very quickly.

DR. ROUSSEL: Thank you.

JUDGE SCHEINER: Thank you for coming in.

(Whereupon, the proceedings at 1:28 p.m. were concluded.)